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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,345	02/15/2006	Graeme Semple	22578-005US1 079.US2.PCT	6159

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EXAMINER	
CHUNG, SUSANNAH LEE	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
10/19/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/535,345	SEMPLE ET AL.	
	Examiner	Art Unit	
	SUSANNAH CHUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4, 7, 10, 11, 14, 17-22, 26-28, 31, 41, and 43-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,7,10,11,14,17-22,26-28,31,41 and 43-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/19/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 4, 7, 10, 11, 14, 17-22, 26-28, 31, 41, and 43-64 are pending in the instant application. Claims 1-3, 5-6, 8-9, 12-13, 15-16, 21-25, 29-30, 32-40, and 42 are canceled.

Information Disclosure Statement

The information disclosure statement (IDS), filed on 8/18/09 has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

RCE

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/18/09 has been entered.

Response

112, 1st rejection

Claims 28-31 were rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims, wherein the instantly claimed compounds are directed to methods of treating a metabolic-related disorder and raising HDL comprising administering to an individual in need of such treatment a therapeutically effective amount of a compound of claim 4.

Applicants response is acknowledged, but is not found persuasive. Applicants argue that (1) the structural difference between niacin and the instantly claimed pyrazole compounds is not the important link and (2) the data on page 57 is directed to the instantly claimed compounds and their biological activity as RUP25 receptor.

It is acknowledged that the link that Applicants are pointing to is the link between both types of compounds to agonize the RUP25 receptor site. This is tied to the data on page 57 of the specification. It is asserted that the data on page 57 does not support the use of the instantly claimed compounds in agonizing the RUP25 receptor site. The data on page 57 states:

> Certain compounds of the invention have an EC_{50} in the ^3H-nicotinic acid binding competition assay within the range of about 10 to about 100 μM. More advantageous compounds of the invention have an EC_{50} value in this assay within the range of about 1 to about 10 μM. Still more advantages compounds have an EC_{50} value in this assay of less than about 1 uM.

Applicants state that this data is for the eleven compounds currently being claimed. The specification states that certain compounds of the invention have an EC50, but the specification does not elaborate which compounds. The specification is vague and it is unclear which compounds have which EC50 value. In view of the vague specification and lack of data supporting the use of the instantly claimed compounds in lowering triglyceride levels it would cause a skilled artisan an undue amount of experimentation to determine if these compounds can lower triglyceride levels.

112, 2nd

Claims 4, 7, 10, 11, 14, 17-22, 26-28, 31 and 41 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds and compositions of claim 4, does not reasonably provide enablement for solvates or hydrates of those compounds. Applicants arguments have been considered, but are not found persuasive. Applicants argue that solvates and hydrates are terms of art and that the burden is on the Office to provide support for why these terms are not enabled. Enclosed is a copy of the Biotechnology, Chemical & Pharmaceutical Customer Partnership Meeting on March 12, 2008.

The definition of solvates from this meeting is "crystalline solid adducts containing solvent molecules within the crystal structure giving rise to unique differences in physical and pharmaceutical properties of the drugs. Hydrates is defined as crystalline solid adducts containing water molecules within the crystal structure. See page 12 of 27.

The following is from the presentation. See page 15 of 27.

Solvates/Hydrates
•It has been estimated that approximately one-third of pharmaceutically active substances are capable of forming hydrates.
•Solvates differ in crystal packing and molecular conformation as well as lattice energy.
•Crystalline states of compounds vs. pharmaceutical compositions may require consideration of phase transformation during formulation of compositions.
·Predicting the formation of solvates and hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of the compound is challenging.

·The reactions and processing involved in the preparation of solvates and hydrates cannot be generalized for a series of related compounds since each solid compound responds uniquely to solvate or hydrate formation

·Pharmaceutical processing (temperature, pressure, relative humidity) encountered during drying, granulation , milling and compression affect crystalline structure, which may make

consistency in products based on structural order difficult to determine and physical properties difficult to maintain.

·Each solid compound responds uniquely to the possible formation of solvates and hydrates and generalizations cannot be made for a series of related compounds

Pharmaceutical processing (temperature, pressure, relative humidity) encountered during drying, granulation , milling and compression affect crystalline structure, making consistency in products based on structural order difficult to determine and maintain.

Consideration of hydration/dehydration of active agents requires consideration of conditions during processing, proper packaging, acceptable temperature ranges for shipping and storage, making selection of the specific solid form of the drug critical.

WANDS FACTOR: Direction provided by the inventor and examples.

Questions of enablement may arise when :
·There are no adequate representations advanced in the specification teaching how to make and use the derivatives such as analogues, prodrugs, metabolites, solvates and hydrates.
·The disclosure fails to direct the skilled artisan to relevant prior art teachings which would correlate modification of a compound in a manner which could be extrapolated to compounds set forth in a patent application's claims.
·When the disclosure does not set forth in full, clear and exact terms the identity and location of modifications to the compound.

Of particular interest, is the statement that an "adequate representations" are required in the specification teaching how to make and use the derivatives such as solvates and hydrates. The instant specification does not have any working examples of solvates or hydrates.

Second, the disclosure does not set forth in full, clear and exact terms the identity and location of the modifications of the compound. It is I known that crystalline states of compounds such as solvates and hydrates can undergo phase transformation and that an exact disclosure of the changes should be disclosed.

Absent data specifying the use of the instantly claimed compounds as solvates or hydrates it would cause a skilled artisan an undue amount of experimentation to determine whether the instantly claimed compounds can be solvates or hydrates and what the pharmacological properties of the solvate and hydrate would be.

Therefore, the claims are rejected because solvate and hydrate is not enabled.

112, 2nd

Claim 41 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants response has been considered and is found persuasive. The admixing step is adequate and this rejection is withdrawn

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Chung whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Susannah Chung/
Examiner, Art Unit 1626